REMARKS

I. STATUS OF THE CLAIMS

Claims 39-69 and 71-80 are pending in the application, of which claims 50, 51, 58, 63-67, 74, and 77-80 are withdrawn from consideration as being drawn to non-elected invention.

Claims 39 and 69 are independent claims, presently under examination.

Claims 39, 40, 42, 44, 45-49, 52-56, 62, 68, 69, 71-73, 75-76 stand rejected under 35 U.S.C. § 102.

Claims 41, 43, 57, 59-61 stand rejected under 35 U.S.C. § 103.

Independent claims 39 and 69 have been amended. Applicants respectfully submit that the proposed amendments to the Claims introduce no new matter and are fully supported by the application as originally filed. Support for the changes are found throughout the Specification, for example, paragraph nos. 46 and 58 as set forth in the present Application Publication, but not limited thereto. Claim 64 and 67 were amended merely to correct dependency.

II. EXAMINER INTERVIEW

Applicants and their representative express their appreciation to the Examiner for the Personal Examiner Interview conducted February 24, 2004.

As per the suggestion of the Examiner, a Declaration under 37 CFR § 1.132 is being filed concurrently herewith.

III. CLAIMS 39, 40, 42, 44, 45-49, 52-56, 62, 68, 69, 71-73, AND 75-76 ARE NOT ANTICIPATED UNDER 35 U.S.C. § 102(b) BY GORDON ET AL. (US 4,862,361); AND CLAIMS 41, 43, 57, AND 59-61 ARE PATENTABLE UNDER 35 U.S.C. § 103 OVER GORDON ET AL. IN VIEW OF SCHROEPPEL (US 6,035,233) ET AL. BECAUSE THE APPLIED PRIOR ART AS A WHOLE FALIS TO SUGGEST THE APPLICANTS' INVENTON.

Claims 39, 40, 42, 44, 45-49, 52-56, 62, 68, 69, 71-73, and 75-76 were rejected under 35 U.S.C. § 102(b) as being anticipated by Gordon et al U.S. Patent No. 4,862,361 (hereinafter

"Gordon"); and claims 41, 43, 57, and 59-61 were rejected under 35 U.S.C. § 103 over Gordon in view Schroeppel et al U.S. Patent No. 6,035,233 (herein after "Schroeppel"). In particular, the Office Action states:

> Claims 39, 40, 42, 44-49, 52-56, 62, 68-69, 71-73 and 75-76 are rejected under 35 U.S.C. 102(b) as being anticipated by Gordon et al. (US4862361). Gordon et al. disclose us of heart rate power spectral analysis to monitor cardiovascular regulation as an indicator of physiological disturbance of the circulatory system homeostasis. Stable and unstable graphic depictions of the parameters are shown in figures 10 and 11 (col. 17, @ 29-41). Stable and unstable data sets graphically charted in figures 16, 17 and 18 show the distribution of heart rate variability data for 29 ill children monitored in a study (col. 23, @ 35-51).
>
> As to claims 39, 40, 42, 44, 47, 49, 54, 56, 62 and 69, Gordon et al. teach a critically ill child may exhibit marked changes in heart rate, read to be heart rate variability, indicative of a major unrecognized pathology. When a child has myocarditis (an inflammation of the muscular walls of the heart incidental to systemic disease), low frequency heart rate fluctuations are seen (col. 4 @ 54 - col. 5 @ 7). The systemic disease as disclosed by Gordon et al. may be a severe systemic infection (col. 26 @ 42-51); it is inherent that severe systemic infections significant for an infant or neonate include necrotizing enterocolitis, pneumonia, sepsis and meningitis.
>
> As to claims 39, 46, 48, 55, 68, 69 and 71-73, the R-R intervals are measured, collecting 1024 points (a ten to the third order data set), and third moment and higher data set is created by a microprocessor using the mean heart rate to calculate a "tachometer waveform" and by using the respiratory peak within a peak and judging the value against a value of two standard deviations from the mean. (col. 5 @ 22 – col. 6, @ 7). The third moment value is recognized as the skewness (specification - page 9, lines 29-31).
>
> As to claims 45, 52, 53, 75 and 76, a mean variance and a maximum of 10% of the heart rate waveform readings is calculated using normalized data (col. 16 @ 64 - col. 17 @ 28).
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> The Applicant's arguments filed 8/21/03 have been fully considered but they are not convincing.
>
> The Applicant argues that since Gordon et al. and the Applicants use an entirely different mathematical approach to detect illness in the infant, the instant invention is not disclosed by Gordon et al.. The Examiner disagrees. In response to the Applicant's arguments that the references fail to show certain features of the Applicant's invention, it is noted that the features upon which the Applicant relies (i.e., real-time monitoring of other kinds of mathematical analyses of heart rate time series (not modified or unmodified power spectra or any other frequency domain parameter); calculating third or higher moment of the heart rate data, as described in the present invention) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The Examiner agrees there are differences in the approaches used by the Applicants and Gordon et al., but as

currently claimed, Gordon et al. and the combination of Gordon et al. and Schroeppel et al. are deemed to read on the claimed invention.

The Applicant makes a general assertion that the Office Action fails to correlate the applied references to the claimed elements. The Examiner disagrees. The Examiner has correlated the elements of the claim with citations in the references. Given the specific elements of concern have not been identified by the Applicant, short of restating the rejection of record, the Examiner is unable to respond to this assertion. As currently claimed, the Gordon et al. and combination of Gordon et al. and Schroeppel et al. are deemed to read on the claimed invention.

(See Office Action, par. 2, pages 2-4)

The Office Action further states:

Claims 41, 43, 57 and 59-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gordon et al. (US 4862361) in view of Schroeppel et al. (US 6035233). As discussed in paragraph 2 of this action, Gordon et al. discloses the claimed invention except for, upon identification of heart rate variability, providing a diagnostic work-up for the illness, including a blood culture or a pathological specimen, and antibiotics to treat the infection.

Schroeppel et al. disclose an implantable device responsive to heart rate variability and teach that, when heart rate variability is identified, it is know to selectively provide increasingly aggressive therapy regimes, beginning with a diagnostic work-up that would inherently include a blood culture and if additional signs of infection were present, such as an elevated temperature, a pathological specimen to identify any potential infection in the lungs or the spinal fluid. Drug therapy is a noted step in the therapy regime; antibiotics are inherent as the drug treatment for an infection (col. 9 @ 3-45). Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the heart rate power spectral analysis as taught by Gordon et al., with the diagnostic work-up for the illness, including a blood culture or a pathological specimen, and antibiotics as taught by Schroeppel et al. to enable diagnosis of the potential fatal illness so effective treatment may be rapidly undertaken to optimize the patient's chances for recovery.

(See Office Action, par. 3, pages 4-5)

Applicants respectfully traverse the rejection of claims 39, 40, 42, 44, 45-49, 52-56, 62, 68, 69, 71-73, 75-76 as being anticipated by Gordon; and submit that claims 41, 43, 57, and 59-61 would not have been obvious under 35 U.S.C. § 103 over Gordon in view of Schroeppel because the applied prior art fails to teach or suggest the following present invention:

i) A method for early detection of subacute, potentially catastrophic illness in an infant, as recited in base claim 39, which calls for:

(a) monitoring frequency histograms of RR intervals in the infant;

(b) identifying at least one characteristic abnormal pattern or distribution; and

(c) correlating the at least one abnormal pattern or distribution with said illness.

ii) An apparatus for early detection of subacute, potentially catastrophic infectious illness in a patient, wherein the patient is an infant, a newborn infant, a toddler, or a child, the apparatus, as recited in base claim 69, which calls for:

(a) a monitoring device, continuously monitoring frequency histograms of RR intervals in the patient; and

(b) a microprocessor, identifying at least one characteristic abnormal pattern or distribution in the RR intervals that is associated with the illness.

A. INTRODUCTION

For purpose of introduction of the prior art, Gordon U.S. Patent No. 4,862,361 (hereinafter "Gordon") teaches real-time monitoring of power spectra of heart rate time series. Thus, a difference between Gordon et al and the present invention is fundamental. Specifically, Gordon et al. use prevalence of various HR frequencies to anticipate illness. Thus, Gordon et al use patterns of *temporal regularity* (frequency) shifting from one state to another. In other words, they state that in health a certain frequency region (regularity of HR) is dominant, while in illness another frequency region (regularity of HR) becomes dominant (with respect to respiratory rate). Therefore Gordon et al rely on micro-level (beat-level) temporal regularity of HR, shifting to another micro-level temporal regularity, to detect illness.

In contrast, the present invention quantifies micro-level (beat-level) *temporal irregularity*. No stable frequencies for any period of time are required to perform these analyses. Therefore the present invention would work in situations when Gordon et al analyses fail (e.g. when there are no apparent periods with certain dominant frequencies).

In short, the present invention has not only a fundamentally different mathematical approach, which does not follow from Gordon's work, but is also based on a fundamentally different physiology underlying HR changes prior to illness. While Gordon's frequency shifts indicate changes in relative parasympathetic-to-sympathetic activity, reduced irregularity of RR

intervals proposed by the present invention indicates greater system isolation and disruption of internal conduits and control mechanisms.

Thus, the present invention describes *inter alia* real-time monitoring of other kinds of physiology of heart rate. Unlike Gordon, the present invention analyses do not calculate modified or unmodified power spectra or any other frequency-domain parameter, and therefore uses entirely different mathematics and approach.

B. RECONSIDERATION

1. In particular, the Office Action (par. 2, page 3) states that Gordon discloses:

...a tachometer waveform and by using the respiratory peak within a peak and judging the value against a value of two standard deviations from the mean.

The Applicants' present invention neither calculates a tachometer waveform, nor does it calculate a respiratory peak to be judged against two standard deviations above the mean.

2. In particular, the Office Action (par. 2, page 3) states that Gordon discloses:

... the R-R intervals are measured, collecting 1024 points (a ten to the third order data set), and third moment and higher data set is created

The Applicants' submit that Gordon invention does not calculate third or higher moments of the heart rate data, as described in the present invention. The Gordon invention mentions calculations of the variance, or second moment, of the RR intervals (c16). This is exclusively in the context of correcting artifacts in the data, and not for interpretation of the clinical status of the patient as in the present invention.

3. The Applicants' submit that the methods taught by Gordon are different than the Applicants' claimed invention. Gordon teaches a frequency domain analysis of a tachometer waveform. The Applicant's claimed invention provides a mathematical analysis based on frequency histogram of the RR intervals. Following Gordon et al, it is impossible to arrive at the present inventions' concept of micro-level temporal irregularity because all Gordon analyses are based on a Fourier transformation of the data, which mathematically eliminates the time axis from the data, leaving only frequency (or period) vs. count (power) axes. The very

mindset of all Fourier-based analyses is looking what happens at specific repeated (and therefore temporally regular) points of the data, not looking at irregularity over time. It is a mathematical impossibility to arrive at any irregularity characteristics as Gordon teaches, e.g. using Fourier analysis - when the data is irregular Fourier analysis would produce a flat spectrum, which yields no information.

In general, Applicants respectfully submit that paragraph 2 of the Office Action has been erroneously applied to the present invention. Moreover, the Office Action fails to correlate the applied references to the claimed elements. Applicants respectfully submit that the prima facie case of obviousness has neither been presented nor achieved by the Office Action. Again, Applicants submit that the applied references are not accurately interpreted by the Examiner.

MPEP §2131 provides:

> "A claim is anticipated only if each and every element as set froth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim.

In view of the differences of base claims 39 and 69 and Gordon, Applicants respectfully urge that the rejections of 40-49, 52-57, 59-62, 68, 71-73 and 75-76 be withdrawn.

Moreover, the Examiner's reliance on Schroeppel does not supply the deficiencies of the Gordon disclosure vis-à-vis Applicants' claims 39 and 69. A dependent claim contains all the limitations of the intermediate claim upon which it depends and is non-obvious under Federal Circuit guidelines if the intermediate claim upon which it depends is allowable. Hence, it is the Applicants' position that the cited art as whole fails to teach or suggest the claimed invention within the meaning of 35 U.S.C. § 103 and request that the rejection of claims 41, 43, 57, and 59-61 be withdrawn.

IV. LEGAL STANDARDS

The legal standards for patentability include novelty and non-obviousness. As affirmed by the Court of Appeals for the Federal Circuit, to support combining references in a §103 rejection, evidence of a suggestion, teaching, or motivation to combine must be clear and particular, and this requirement is not met by merely offering broad, conclusory statements about teachings of references. *In re Dembiczak*, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999); *In re Sang Su Lee*, 61 USPQ 2d 1430, 1435 (Fed. Cir. 2002). Further, "[i]t is insufficient to establish obviousness that the separate elements of the invention existed in the prior art, absent some teaching or suggestion, in the prior art, to combine the elements." *Arkie Lures, Inc. v. Gene Larew Tackle, Inc.*, 43 USPQ2d 1294, 1297 (Fed. Cir. 1997) (emphasis added). The standard of obviousness is not whether, in hindsight, someone would have combined elements to form the invention. *W.L. Gore & Associates v. Garlock, Inc.*, 220 USPQ 303, 312-313 (Fed. Cir. 1983). Applicants reiterate that, properly combined, the cited references fail to teach or suggest the claimed invention. In view of the foregoing, Applicant respectfully requests that the obviousness rejections be withdrawn.

V. CONCLUSION

For the foregoing reasons, Applicants respectfully submit that claims 39-49, 52-57, 59-62, 68, 69, 71-73, 75-76 are in condition for allowance, and a notice for allowance is solicited. Should questions arise during examination, the Examiner is welcome to contact the Applicants' attorney at the telephone listed below.

Please charge any excess fees due and credit any overpayment to Charge Account No. 50-0423.

Respectfully submitted,

Date: March 17, 2004

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